

10/552363  
JC05 Rec'd PCT/PTO 03 OCT 2005

Patent - PCT  
Docket: 50821/14 PCT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY - US

EXPRESS MAIL LABEL NO.: ER 620043240 US

Applicants:

NPS PHARMACEUTICALS, INC.  
GLAXOSMITHKLINE  
IRINA V. SHCHERBAKOVA  
MANUEL F. BALANDRIN  
GUANGFEI HUANG  
OTTO GEOFFROY  
JOHN FOX  
ROBERT MARQUIS  
DENNIS SHINJI YAMASHITA  
JUAN LUENGO  
WENYONG WANG

Inventors:

IRINA V. SHCHERBAKOVA  
MANUEL F. BALANDRIN  
GUANGFEI HUANG  
OTTO GEOFFROY  
JOHN FOX  
ROBERT MARQUIS  
DENNIS SHINJI YAMASHITA  
JUAN LUENGO  
WENYONG WANG

International  
Application No.:

PCT/US2004/010638

Title:

PYRIMIDINONE COMPOUNDS AS  
CALCILYTICS

International  
Filing Date:

7 April 2004 (07.04.2004)

Priority Date:

7 April 2003 (07.04.2003)

Attorney  
Docket No.:

50821/14 PCT

AMENDMENT PURSUANT TO ARTICLE 34(2)(b) AND RULE 66.1,  
WITH ACCOMPANYING STATEMENT PURSUANT TO ARTICLE 19(1)  
AND RULE 46.4, IN RESPONSE TO FIRST WRITTEN OPINION

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Attention: Deepak Rao  
Authorized Officer

Dear Deepak Rao:

Responsive to the first Written Opinion mailed 15 February 2005 and having a term of reply of 15 May 2005, applicant respectfully submits this amendment and statement and requests reconsideration of the claims as amended.

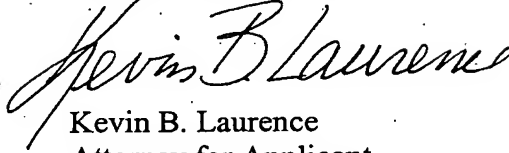
The claims as contained on the accompanying substitute pages 46-55 include amendments to independent claim 1 and dependent claim 9. Specifically, the claims as amended recite that  $R^4$  is a group of the formula  $-(CH_2)_n-R^5$  wherein  $n$  is 1 or 2 and  $R^5$  is an aryl group.

The Written Opinion cites EP 579424 against claims 1-10 as lacking novelty and inventive step under PCT Article 33(2) and 33(3), respectively. However, EP 579424 does not disclose or fairly suggest compounds that have an  $R^4$  group with the formula  $-(CH_2)_n-R^5$  wherein  $n$  is 1 or 2 and  $R^5$  is an aryl group. Instead EP 579424 discloses an  $R^4$  group having a lower alkyl. A lower alkyl does not teach or suggest an aryl group bonded to  $-(CH_2)_n-$ . Therefore, the claims as amended meet the criteria of novelty and inventive step set out in PCT Article 33(2)-(3).

Since it appears that the rejections and objections noted in the written opinion have been overcome, the amendments presented herein are believed to place these claims and the specification in condition for a favorable preliminary examination report holding all claims patentable under PCT articles 33 and 6 and therefore favorable reconsideration is respectfully requested.

DATED this 47<sup>th</sup> day of April, 2005.

Respectfully submitted,

A handwritten signature in cursive script that reads "Kevin B. Laurence".

Kevin B. Laurence  
Attorney for Applicant  
Registration No. 38,219

STOEL RIVES LLP  
One Utah Center  
201 So. Main Street, Suite 1100  
Salt Lake City, Utah 84111  
Telephone: (801) 328-3131

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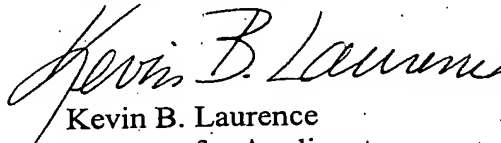
Date of Deposit:

April 4, 2005

I hereby certify that the enclosed AMENDMENT PURSUANT TO ARTICLE 34(2)(b) AND RULE 66.1, WITH ACCOMPANYING STATEMENT PURSUANT TO ARTICLE 19(1) AND RULE 46.4, IN RESPONSE TO FIRST WRITTEN OPINION for filing in the matter of the Application of NPS Pharmaceuticals, Inc., et al, for PYRIMIDINONE COMPOUNDS AS CALCILYTICS, Serial No. PCT/US2004/010638, International filing date 7 April 2004, Priority Date 7 April 2003, is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10 on the date indicated above in an envelope addressed to the Commissioner for Patents, Attention: Deepak Rao, Authorized Officer, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Respectfully submitted this 4<sup>TH</sup> day of April, 2005.

Respectfully submitted,



Kevin B. Laurence  
Attorney for Applicant  
Registration No. 38,219

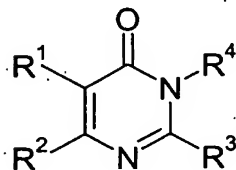
STOEL RIVES LLP  
One Utah Center  
201 So. Main Street, Suite 1100  
Salt Lake City, Utah 84111  
Telephone: (801) 328-3131

KBL:js

Attorney Docket: 11502/14 PCT

## Claims

1. A compound having the chemical formula:



wherein:

R<sup>1</sup> and R<sup>2</sup> are either independently one of: H, halogen, CN, CF<sub>3</sub>, lower alkyl, cycloalk, and aryl; or R<sup>1</sup> and R<sup>2</sup> are together -(CH<sub>2</sub>)<sub>n</sub>- and n is 5, 4, or 3;

R<sup>3</sup> is aryl group, which may have 1 to 4 substituents in the aryl ring and each substituent is one of: H, halogen, CN, CF<sub>3</sub>, OCF<sub>3</sub>, lower alkyl, N(lower alkyl)<sub>2</sub>, lower alkoxy, OH, OC(O)-lower alkyl, OC(O)-lower alkylamino, and OC(O)-lower alkyl-N(lower alkyl)<sub>2</sub>;

R<sup>4</sup> is a group of the formula -(CH<sub>2</sub>)<sub>n</sub>-R<sup>5</sup> wherein n is 1 or 2, and R<sup>5</sup> is an aryl group which may have 1 to 3 substituents on the aryl ring and each substituent is one of: H, halogen, CN, CF<sub>3</sub>, OCF<sub>3</sub>, lower alkyl, lower alkoxy, NH-lower alkyl, NH-alkylaryl, N(lower alkyl)<sub>2</sub>, OH, OC(O)-lower alkyl, OC(O)-lower alkylamino, and OC(O)-lower alkyl-N(lower alkyl)<sub>2</sub>;

and pharmaceutically acceptable salts or complexes.

2. The compound according to claim 1, wherein R<sup>1</sup> and R<sup>2</sup> are independently one of hydrogen and lower alkyl.

3. The compound according to claim 1, wherein R<sup>1</sup> and R<sup>2</sup> are together -(CH<sub>2</sub>)<sub>n</sub>- and wherein n is 4 or 3.

4. The compound according to claim 2, wherein said lower alkyl is one of: methyl, ethyl and isopropyl.

5. The compound according to claim 1, wherein R<sup>1</sup> is one of ethyl and isopropyl.

6. The compound according to claim 1, wherein R<sup>2</sup> is methyl.

7. The compound according to claim 3, wherein R<sup>1</sup> and R<sup>2</sup> together are – (CH<sub>2</sub>)<sub>4</sub>–.

8. The compound according to claim 1, wherein R<sup>3</sup> is phenyl optionally substituted with one of hydroxy or hydroxy and fluorine.

9. The compound according to claim 1, wherein R<sup>5</sup> is phenyl optionally substituted with 1 or 2 halogens.

10. The compound according to claim 9, wherein n is 2 and said halogens are one of fluorine and chlorine.

11. The compound according to claim 1, wherein the compound is at least one of:

2-(2-hydroxy-phenyl)-6-methyl-3-phenethyl-3*H*-pyrimidin-4-one;

3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-5,6-dimethyl-3-phenethyl-3*H*-pyrimidin-4-one;

3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

3-[2-(4-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

5-ethyl-2-(2-hydroxy-phenyl)-6-methyl-3-phenethyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(4-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-5-propyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5-isopropyl-6-methyl-3*H*-pyrimidin-4-one;

3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5-isopropyl-6-methyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-5-methyl-3-phenethyl-6-trifluoromethyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-3-phenethyl-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one;

5-cyclopropyl-3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-3-phenethyl-3,5,6,7-tetrahydro-cyclopentapyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-3,5,6,7-tetrahydro-cyclopentapyrimidin-4-one;

5-ethyl-2-(2-methoxy-phenyl)-6-methyl-3-phenethyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-5-isopropyl-2-(2-methoxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

2-(5-chloro-2-hydroxy-pyridin-3-yl)-5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-2-(3-fluoro-2-hydroxy-phenyl)-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-2-(5-fluoro-2-hydroxy-phenyl)-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-2-(2-fluoro-6-hydroxy-phenyl)-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one;

2-(5-chloro-2-hydroxy-phenyl)-5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one;

2-(5-bromo-2-hydroxy-phenyl)-5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-3-isopropyl-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

2-(3,5-dibromo-2-hydroxy-phenyl)-5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-2-(3-chloro-2-hydroxy-phenyl)-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-3-methyl-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

2-(4-chloro-2-hydroxy-phenyl)-5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-4-methoxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one.

12. The compound according to claim 1, wherein the compound is at least one of:

2-(2-hydroxy-phenyl)-6-methyl-3-phenethyl-3*H*-pyrimidin-4-one;

3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-5,6-dimethyl-3-phenethyl-3*H*-pyrimidin-4-one;

3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

3-[2-(4-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

5-ethyl-2-(2-hydroxy-phenyl)-6-methyl-3-phenethyl-3*H*-pyrimidin-4-one;



5-ethyl-3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(4-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-5-propyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5-isopropyl-6-methyl-3*H*-pyrimidin-4-one;

3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5-isopropyl-6-methyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-5-methyl-3-phenethyl-6-trifluoromethyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-3-phenethyl-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one;

5-cyclopropyl-3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-3-phenethyl-3,5,6,7-tetrahydro-cyclopentapyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-3,5,6,7-tetrahydro-cyclopentapyrimidin-4-one;

5-ethyl-2-(2-methoxy-phenyl)-6-methyl-3-phenethyl-3*H*-pyrimidin-4-one;

2-(5-chloro-2-hydroxy-pyridin-3-yl)-5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-2-(3-fluoro-2-hydroxy-phenyl)-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-2-(5-fluoro-2-hydroxy-phenyl)-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-2-(2-fluoro-6-hydroxy-phenyl)-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one;

2-(5-bromo-2-hydroxy-phenyl)-5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-3-isopropyl-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

2-(3,5-dibromo-2-hydroxy-phenyl)-5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one; and

2-(4-chloro-2-hydroxy-phenyl)-5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one.

13. The compound according to claim 1, wherein the compound is at least one of:

2-(2-hydroxy-phenyl)-6-methyl-3-phenethyl-3*H*-pyrimidin-4-one;

3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-5,6-dimethyl-3-phenethyl-3*H*-pyrimidin-4-one;

3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

3-[2-(4-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

5-ethyl-2-(2-hydroxy-phenyl)-6-methyl-3-phenethyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(4-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-5-propyl-  
 3*H*-pyrimidin-4-one;  
 3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5-isopropyl-6-methyl-  
 3*H*-pyrimidin-4-one;  
 3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5-isopropyl-6-methyl-  
 3*H*-pyrimidin-4-one;  
 2-(2-hydroxy-phenyl)-5-methyl-3-phenethyl-6-trifluoromethyl-3*H*-  
 pyrimidin-4-one;  
 2-(2-hydroxy-phenyl)-3-phenethyl-5,6,7,8-tetrahydro-3*H*-quinazolin-4-  
 one;  
 3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6,7,8-tetrahydro-  
 3*H*-quinazolin-4-one;  
 5-cyclopropyl-3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-  
 methyl-3*H*-pyrimidin-4-one;  
 2-(2-hydroxy-phenyl)-3-phenethyl-3,5,6,7-tetrahydro-  
 cyclopentapyrimidin-4-one;  
 3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-3,5,6,7-tetrahydro-  
 cyclopentapyrimidin-4-one;  
 5-ethyl-2-(3-fluoro-2-hydroxy-phenyl)-3-[2-(3-fluoro-phenyl)-ethyl]-6-  
 methyl-3*H*-pyrimidin-4-one;  
 5-ethyl-2-(5-fluoro-2-hydroxy-phenyl)-3-[2-(3-fluoro-phenyl)-ethyl]-6-  
 methyl-3*H*-pyrimidin-4-one;  
 5-ethyl-2-(2-fluoro-6-hydroxy-phenyl)-3-[2-(3-fluoro-phenyl)-ethyl]-6-  
 methyl-3*H*-pyrimidin-4-one; and  
 2-(4-chloro-2-hydroxy-phenyl)-5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-6-  
 methyl-3*H*-pyrimidin-4-one.

14. The compound according to claim 1, wherein the compound is at least one of:

2-(2-hydroxy-phenyl)-5,6-dimethyl-3-phenethyl-3*H*-pyrimidin-4-one;  
 3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-  
 pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

3-[2-(4-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6-dimethyl-3*H*-pyrimidin-4-one;

5-ethyl-2-(2-hydroxy-phenyl)-6-methyl-3-phenethyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-3-[2-(4-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-5-propyl-3*H*-pyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5-isopropyl-6-methyl-3*H*-pyrimidin-4-one;

3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5-isopropyl-6-methyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-5-methyl-3-phenethyl-6-trifluoromethyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-3-phenethyl-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-5,6,7,8-tetrahydro-3*H*-quinazolin-4-one;

5-cyclopropyl-3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one;

2-(2-hydroxy-phenyl)-3-phenethyl-3,5,6,7-tetrahydro-cyclopentapyrimidin-4-one;

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-3,5,6,7-tetrahydro-cyclopentapyrimidin-4-one;

5-ethyl-2-(3-fluoro-2-hydroxy-phenyl)-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one;

5-ethyl-2-(5-fluoro-2-hydroxy-phenyl)-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one; and

5-ethyl-2-(2-fluoro-6-hydroxy-phenyl)-3-[2-(3-fluoro-phenyl)-ethyl]-6-methyl-3*H*-pyrimidin-4-one.

15. The compound according to claim 1, wherein the compound is at least one of:

5-ethyl-3-[2-(2-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-3*H*-pyrimidin-4-one; and

3-[2-(3-fluoro-phenyl)-ethyl]-2-(2-hydroxy-phenyl)-6-methyl-5-isopropyl-3*H*-pyrimidin-4-one.

16. A pharmaceutical composition comprising a compound according to claim 1 and a pharmaceutically acceptable diluent or excipient.

17. A method of treating a disease or disorder characterized by abnormal bone or mineral homeostasis which comprises the administration to a subject in need of treatment thereof an effective amount of a compound according to claim 1.

18. A method according to claim 17, wherein the bone or mineral disease or disorder is selected from the group consisting of osteosarcoma, periodontal disease, fracture healing, osteoarthritis, rheumatoid arthritis, Paget's disease, humoral hypercalcemia malignancy, and osteoporosis.

19. A method according to claim 17, wherein the bone or mineral disease or disorder is osteoporosis.

20. A method of increasing serum parathyroid hormone levels in mammals, which comprises the administration to a subject in need of treatment thereof an effective amount of a compound according to claim 1.

#### Abstract of the Disclosure

The pyrimidinone compounds are disclosed. Methods of preparing the pyrimidinone compounds are also disclosed.